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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,295	03/22/2004	Paulo LaColla	06171.105033 (IDX 1008 DI	1837

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EXAMINER	
WILLIAMS, LEONARD M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/806,295	LACOLLA ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-24,27-46 and 49-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-24,27-46 and 49-56* is/are rejected.

7)☒ Claim(s) *57-64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/1/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant's election without traverse of Group III, drawn to a method of treatment or prophylaxis of HIV infection, in the reply filed on August 15, 2005 is acknowledged. Claims 8, 9, 12, 13, 25 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. The species requirement set forth in the restriction requirement dated July 12, 2005 is hereby withdrawn.

Response to Amendments/Arguments

The amending of claims 19-20, 23-24 and 27-28 to remove the term "or prophylaxis" is sufficient to overcome the 112-1 rejection of claims 19-24 and 27-28 and thus the 112-1 rejection is withdrawn.

Applicant's arguments filed 02/06/2006 have been fully considered but they are moot due to the withdrawal of the 103(a) rejection of record as necessitated by applicant's amendment. A rejection encompassing the claims as amended is detailed below.

The applicants traverse the 103(a) rejection of claims 19-24, 27-32, 45, 47-51 and 53-56 over Williams et al. (USPN 5527819, hereafter '819) on the grounds that the currently claimed compounds are not obvious homologs of Williams' et al. claimed compounds, and that there is no suggestion that additional substitution of the indole ring

would yield compounds active against HIV infection. Further applicant's say one of ordinary skill in the art would be motivated away from additional substitution on the indole ring due to Williams' et al. lack of teaching more than one subsistent. The examiner respectfully disagrees. The lack of teaching of additional substitutions on the indole ring of Williams et al. does not preclude that compounds with additions to the indole ring would maintain/enhance or even decrease the individual compound's activity against HIV. Indeed Williams et al. is silent in regards to additional substitution of the indole ring. The examiner wishes to point out that on page 86 of the current specification the applicant's disclose compound 1 wherein R=H and R1=NH2 and disclose activity of said compound in a series of p24 HIV-1 assays. The examiner wishes to note that said compound 1 is identical to compound 18 as disclosed by Williams et al. (see column 11 lines 5-15). Further the examiner wishes to note that the activity profile of the compounds disclosed in Table 1 on page 86 of the current application indicate that compound 1 is more active than compound 2 wherein R=3,5 diMe. Thus current compound 1 as disclosed by applicants is the same compound as compound 18 of Williams et al. and indicates that substitution of R from H to 3,5-diMe decreases the activity of the compound. The applicant's further show in Tables 2 and 3 activities of other R=3,5diMe compounds in a variety of HIV assays and even against resistant HIV strains but do not show the activity profile of compound 1 in any of the assays (see Tables 2 and 3). This is especially important of note in regards to Table 3 where the R1 substituents are di-halo indole compounds. The applicant's do not compare a mono-halo compound (such as compound 1) against a homologous di-halo

compound (such as compound 8) wherein the only difference is the addition of the second halo group.

On page 36 of the remarks, the applicant's point the examiner to an article by Balani in order to provide support for the teaching away of multiple substitutions of the indole ring by pointing out the inactivity of metabolites of compound L-734005 (respectively compound M2B). The examiner respectfully points out both L-734005 and M2B are not equivalent compounds to the present invention or the compounds of Williams et al. as discussed. For example both L-734005 and M2B are alkylthio indole compounds and not alkyl sulfoxide compounds. Further on page 600 of Balani it is taught that the sulfoxide metabolite M3 (which is equivalent to applicant's compound 1 and Williams et al. compound 18) is ~7 fold more active than the parent compound L-734005. Thus this reference teaches that the sulfoxide functionality is important for increased activity and that the addition of a hydroxyl group to the alkylthio-indole moiety of L-734005 diminishes (or abolishes activity). As pointed out before there are no direct homologous comparisons.

Due to the applicant's amendment the 103(a) rejection of the previous office action is withdrawn and a rejection encompassing the claims as amended follows.

Claim Objections

Claims 57-64 are objected to because of the following informalities: Claims 57-64 are dependent on rejected claims 19 and 24. Rewriting the claims to independent

form including all limitations of the base claims is suggested. Appropriate correction is required.

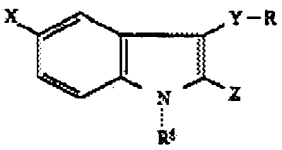
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-24, 27-32, 45, 47-51 and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. (USPN 5527819).

Williams et al. teaches inhibitors of HIV reverse transcriptase for the treatment of HIV infection with the formula:



R is taught to be an aryl with the same substituents as claimed. Y is taught to be $S(O)_n$ or O, as claimed. Z is selected from various amides, imines, etc., as claimed. R6 is taught to be selected from, e.g., hydrogen, as claimed. X is taught to be selected from H, Cl, F, BR, etc., as claimed. Treatment of HIV in combination with other anti-HIV agents is also taught. See Abstract; col. 1, line 14-col. 15, line 23. Williams et al. does not teach at least one of $R^{4'}$, $R^{6'}$ or $R^{7'}$ as a non-hydrogen atom.

It would have been obvious to one of ordinary skill in the art to utilize a compound, as claimed wherein $R^{4'}$, $R^{6'}$ or $R^{7'}$ is a non-hydrogen because adjacent homologs are considered to be obvious absent unexpected results (*In re Henze*, 85 USPQ 261, 263 CCPA 1950) and members of a homologous series must possess unexpected properties not possessed by the homologous compounds disclosed by the prior art. *In re Hass*, 141 F.2d 127, 60 USPQ 548 CCPA 1944. *In re Hass*, 141 F.2d 127, 60 USPQ 548 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950). In the instant case Applicant has claimed adjacent homologs to those taught in Williams et al. because Applicant's claimed invention encompasses a treatment wherein any one of $R^{4'}$, $R^{6'}$ or $R^{7'}$ is a methyl group or an halo group. With the teaching of Williams et al., one of ordinary skill in the art would expect to achieve at least similar results in the treatment of an HIV infection with the compounds of the invention disclosed therein when one of hydrogen atoms at the 4, 6 or 7 positions of the indole group are substituted with a methyl or halo group. Furthermore, it is noted that since Williams et al. teaches the treatment of HIV in general, it would have been obvious to one of ordinary skill in the art to treat specific instances of HIV, including those as claimed.

It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to

any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972).

Conclusion

Claims 57-64 appear to be free of the art.

Claims 57-64 would be allowable if rewritten in an independent form to include all of the limitations of the base claim and any intervening claims.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER